

"Replacement Sheet"

The Human E3 α Ubiquitin Ligase Family

Han et al. - Appl. No. 10/758,672

Atty Docket: 01017/35966B

Fig. 1A (Page 1 of 23)

SEQ ID NO:

Figure 1A

6 mouse_E3 α I MASEMEPEVQ AID-RSLLC SAEIAGRML QATDLNREY QHLAHCVPKI 49
4 human_E3 α I MASELEPEVQ AID-RSLLC SAEIAGKWL QATDLTREY QHLAHYVPKI 49
15 mouse_E3 α I MADEMDGAE RMDVSPEPL APQRPASWMD QQVDFYTAFL HHLAQLVPEI 50
2 human_E3 α I MADEAGGTE RMEISAEPLQ TPQRLASWMD QQVDFYTAFL HHLAQLVPEI 50
Consensus MA.E.....D....L.....A.W.Q.D.....HLA..VP.I 50

6 mouse_E3 α I YCRGNPFPQ KEDTLAQHLL LGPMEWICA EDPALGFPKL EQANKPSHLC 99
4 human_E3 α I YCRGNPFPQ KEDMLAQHVL LGPMEWLCG EDPAFGFPKL EQANKPSHLC 99
15 mouse_E3 α I YFAEMDPDL KQESVQMSI LTPLEWLFGE EDPDICLEKL KHSG-AFQLC 99
2 human_E3 α I YFAEMDPDL KQESVQMSI FTPLWLFGE EDPDICLEKL KHSG-AFQLC 99
Consensus Y.....P....K.....Q...L.P.EWVL.GEDP.....KL.....LC 100

6 mouse_E3 α II GRVFKVGEPT YSCRDCAVDP TCVLMECFLL GSIHRDHRMR MTTSGGGGFC 149
4 human_E3 α II GRVFKVGEPT YSCRDCAVDP TCVLMECFLL GSIHRDHRMR MTTSGGGGFC 149
15 mouse_E3 α I GKVFKSGETT YSCRDCAI DP TCVLCMDCFQ SSVHKNHRYK MHTSGGGFC 149
2 human_E3 α I GRVFKSGETT YSCRDCAI DP TCVLCMDCFQ DSVHKNHRYK MHTSGGGFC 149
Consensus GRVFK.GE.TYSCRDCA.DP.TCVLCMCF...S.H.HRY.M.TS.GGGFC 150

6 mouse_E3 α II DCGDTEAWKE GPRYCKHKLSSSEVEEEDP LVHLSEDAIA RTYNI FAIMF 199
4 human_E3 α II DCGDTEAWKE GPRYCKHKLSSSEVEEEDP LVHLSEDAIA RTYNI FAIMF 199
15 mouse_E3 α I DCGDTEAWKT GPFCDVHEPG RAGTKESLH -CPLNEEVI A QARRIFPSVI 198
2 human_E3 α I DCGDTEAWKT GPFCDVHEPG RAGTKESLH -CPLNEEVI A QARRIFPSVI 198
Consensus DCGDTEAWK.GP.C.HE.....E...L.E.VIA...IF.... 200



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Fig. 1B (Page 2 of 23)

Figure 1B

6	mouse_E3 α II	RYAVDILTWE	KESELPEDLE	VAEKSDTYYC	MLFNDEVHTY	EQVIYTLQKA	249
4	human_E3 α II	RYAVEILTWE	KESELPADLE	MEEKSDTYYC	MLFNDEVHTY	EQVIYTLQKA	249
15	mouse_E3 α I	KYI VEMTI WE	EKELPELO	I REKNERYYC	VLFNDEHHSY	DHVIYSLQRA	248
2	human_E3 α I	KYVEMTI WE	EKELPELO	I REKNERYYC	VLFNDEHHSY	DHVIYSLQRA	248
	Consensus	.Y.VE...WE	.E.ELP.L.	..EK...YYC	.LFNDE.H.Y	..VIY.LQ.A	250
6	mouse_E3 α II	VNCTQKEAIG	FATTVDRDGR	RPVRYGDFQY	CDQAKTIVIR	NTSRQTK-PL	298
4	human_E3 α II	VNCTQKEAIG	FATTVDRDGR	RSVRYGDFQY	CEQAKSVIR	NTSRQTK-PL	298
15	mouse_E3 α I	LDCELAEAQL	HTTAIDKEGR	RAVKAGVYAT	COEAKEDIKS	HSENVSQHPL	298
2	human_E3 α I	LDCELAEAQL	HTTAIDKEGR	RAVKAGAYAA	COEAKEDIKS	HSENVSQHPL	298
	Consensus	..C...EA.	..T..D..GR	R.V..G....	C..AK..I..PL	300
6	mouse_E3 α II	KVQVMHSSVA	AHQNFGLKAL	SWLGSVIGYS	DGLRRLICQV	GLQEGPDGEN	348
4	human_E3 α II	KVQVMHSSI V	AHQNFGLKLL	SWLGSII GYS	DGLRRLICQV	GLQEGPDGEN	348
15	mouse_E3 α I	HVEVLHSVVM	AHQKFALRLG	SWANKIMSYS	SDFRQIFCQA	CLVEEPGSEN	348
2	human_E3 α I	HVEVLHSEIM	AHQKFALRLG	SWANKIMSYS	SDFRQIFCQA	CLREPPDSEN	348
	Consensus	.V.V.HS...	AHQ.F.L.L.	SW...I...YS	...R.I.CQ.	.L.E.PD.EN	350

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Fig. 1C (Page 3 of 23)

Figure 1C

6	mouse_E3 α I	SSLVDRLMLN DSKLWKGARS VYHQLFMSL LMDLKYKKLF ALRF AKNYRQ	398
4	human_E3 α II	SSLVDRLMS DSKLWKGARS VYHQLFMSL LMDLKYKKLF AVRF AKNYQQ	398
15	mouse_E3 α I	PCLISRLMW DAKLYKGARK LHELI FSSF FME MEYKKLF AMEFVKYKQ	398
2	human_E3 α I	PCLISRLMW DAKLYKGARK LHELI FSSF FME MEYKKLF AMEFVKYKQ	398
	Consensus	..L..RLM. D.KL.KGAR. ..H.L..SS. .M..YKKLF A..F.K.Y.Q	400
6	mouse_E3 α II	LQRDFMEDDH ERAVSVTALS VQFFTAPTLA RMLTEENLM TVI I KAFMDH	448
4	human_E3 α II	LQRDFMEDDH ERAVSVTALS VQFFTAPTLA RMLTEENLM SII I KTFMDH	448
15	mouse_E3 α I	LQKEYI SDDH ERSI SITALS VQMLTVPTLA RHLIEEQNVI SVI TETLLEV	448
2	human_E3 α I	LQKEYI SDDH DRSI SITALS VQMTVP TLA RHLIEEQNVI SVI TETLLEV	448
	Consensus	LQ.....DDH ER..S.TALS VQ.FT.PTLA R.LI.E.N..SVI..T...	450

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Fig. 1D (Page 4 of 23)

Figure 1D

SEQ ID NO:

6	mouse_E3 α II	LKHRDAQGRF	QFERYTALQA	FKFRRVQSLI	LDLKYVLISK	PTWSDLRQ	498
4	human_E3 α II	LRHRDAQGRF	QFERYTALQA	FKFRRVQSLI	LDLKYVLISK	PTWSDLRQ	498
15	mouse_E3 α I	LPEYLDNRN-	KFN-FQGSQ	DKLGRVYAVI	CDLKYILISK	PVIWTERLRA	496
2	human_E3 α I	LPEYLDNRN-	KFN-FQGSQ	DKLGRVYAVI	CDLKYILISK	PTIWTERLRM	496
	Consensus	L.....	.F.....	.K..RV...I	.DLKY.LISK	PT.W..LR.	500
6	mouse_E3 α II	KFLQGFDAFL	ELLKCMQGM	PI TRQVGQHI	EMEPWEAAF	TLQMKLTHVI	548
4	human_E3 α II	KFLQGFDAFL	ELLKCMQGM	PI TRQVGQHI	EMEPWEAAF	TLQMKLTHVI	548
15	mouse_E3 α I	QFLEGFRSFL	KILTCMQME	EI RROVGQHI	EVDPDWEAAI	AI QMLKNIL	546
2	human_E3 α I	QFLEGFRSFL	KILTCMQME	EI RROVGQHI	EVDPDWEAAI	AI QMLKNIL	546
	Consensus	.FLEGF..FL	..L.CMQGM	.I.RQVGQHI	E..P.WEAA.	..QML....	550
6	mouse_E3 α II	SMWQDWALD	EKVLIEAYKK	CLAVLTQCHG	GFTDGEQPI T	LSICGHSVET	598
4	human_E3 α II	SMWQDWALD	EKVLIEAYKK	CLAVLTQCHG	GFTDGEQPI T	LSICGHSVET	598
15	mouse_E3 α I	LMFQEWACAD	EDLLLVAYKE	CHKAVMRCST	NFMSTKTIV-	VQLCGHSLET	595
2	human_E3 α I	LMFQEWACAD	EELLVAYKE	CHKAVMRCST	SFISSTKTIV-	VOSCGHSLET	595
	Consensus	.M.Q.WCA.D	E..L..AYK.	C....M.C..	.F.....	...CGHS.ET	600

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Figure 1E

6	mouse_E3 α I	I RYCVSQEKV SI HLPISRL AGLHVLSSKS EVAYKPELL PLSLSPPL	648
4	human_E3 α I	I YCVSQEKV SI HLPVSRLL AGLHVLSSKS EVAYKPELL PLSLSPPL	648
15	mouse_E3 α I	KSYKVSIEDLV SI HLPISRTL AGLHVRLSRL GAI SRLHEFV PFDSFQEV	645
2	human_E3 α I	KSYRVSEDLV SI HLPISRTL AGLHVRLSRL GAVSRLHEFV SFEDFQEV	645
	Consensus	..Y.VS...V SI HLP.SR.L AGLHV.LS... ..E.. P.....L	650
6	mouse_E3 α II	I EHPLRCLVL CAQVHAGMAR RNGFSLVNOI YYYHNVKCR EMDKDI VML	698
4	human_E3 α II	I EHPLRCLVL CAQVHAGMAR RNGFSLVNOI YYYHNVKCR EMDKDVML	698
15	mouse_E3 α I	VEYPLRCLVL VAQVVAEMMR RNLGLSIQV FYYQDVKCRE EMDKDI I ML	695
2	human_E3 α I	VEYPLRCLVL VAQVVAEMMR RNLGLSIQV FYYQDVKCRE EMDKDI I ML	695
	Consensus	.E.PLRLCLVL .AQV.A.MMR RNG.SL..Q..YY..VKCR. EM.DKDI.ML	700
6	mouse_E3 α II	QTGVSMDPN HFLM M.SRF ELYQLFSTPD YGKRFSSEVT HKDVQQNNT	748
4	human_E3 α II	QTGVSMDPN HFLM M.SRF ELYQI FSTPD YGKRFSSEIT HKDVQQNNT	748
15	mouse_E3 α I	QI GASI MDPN KFLLLVLRQY EL-----TDA FNKTI ST--K DQDLI KQYNT	738
2	human_E3 α I	QI GASLMDPN KFLLLVLRQY EL-----AEA FNKTI ST--K DQDLI KQYNT	738
	Consensus	Q.G.S.MDPN .FL...L.R. EL.....T... ..K..S.... ..D...Q.NT	750

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Figure 1F

6	mouse_E3 α II	LI EEM YLI I	ML VGER F NPG	VGQVATDEI	KREI I HQLSI	KPMAHSELVK	798
4	human_E3 α II	LI EEM YLI I	ML VGER F SPG	VGQVATDEI	KREI I HQLSI	KPMAHSELVK	798
15	mouse_E3 α I	LI EEM QVLI	YI VGER YVPG	VGNVTREEVI	MREI THLCI	EPMPHSAI AR	788
2	human_E3 α I	LI EEM QVLI	YI VGER YVPG	VGNVTKEEVT	MREI I HLICI	EPMPHSAI AK	788
	Consensus	LI EEM . . . I	. . VGER . . PG	VG . V I	. REI I H . L . I	. PM HS . . . K	800
6	mouse_E3 α II	SLPEDENKET	GMESVI ESVA	HFKKPGLTGR	GMVELKPECA	KEFNLYFYHF	848
4	human_E3 α II	SLPEDENKET	GMESVI EAVA	HFKKPGLTGR	GMVELKPECA	KEFNLYFYHF	848
15	mouse_E3 α I	NLPENENNENET	GLENNI NKVA	TFKKPGVSGH	GVYELKDESL	KDFNMFFYHY	838
2	human_E3 α I	NLPENENNENET	GLENNI NKVA	TFKKPGVSGH	GVYELKDESL	KDFNMFFYHY	838
	Consensus	. LPE . EN . ET	G . E . VI . . VA	. FKKPG . G .	G . YELK . E . .	K . FN . YFYH .	850
6	mouse_E3 α II	SRAEQSKAE	AQRKLKRENK	EDTALPPAL	PPFCPLFASL	VNLLQCDVM	898
4	human_E3 α II	SRAEQSKAE	AQRKLKRONR	EDTALPPVL	PPFCPLFASL	VNLLQSDVM	898
15	mouse_E3 α I	SKTOHSKAEH	MQKKRKRQEN	KDEALPPPP	PEFCPAFSKV	VNLLSCDVM	888
2	human_E3 α I	SKTOHSKAEH	MQKKRKRQEN	KDEALPPPP	PEFCPAFSKV	INLLNCIDIMM	888
	Consensus	S SKAE .	. Q . K . . . Q . .	. D . ALPPP . .	P . FCP . F . . .	VN . L . CDVM	900

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Figure 1G

SEQ ID NO:

6 mouse_E3 α II YI MGTI LQWA VEHNGSAWSE SMLQRVLHLI GMALQEEKHH LENAVEGHVQ 948
 4 human_E3 α II CIMGTI LQWA VEHNGYAWSE SMLQRVLHLI GMALQEEKOH LENVTEEHV 948
 15 mouse_E3 α I YILRTIFERA VDESNLWTE GMLQMAFHIL ALGLLEEKQQ LQAPPEEV- 937
 2 human_E3 α I YILRTVFERA IDTDSNLWTE GMLQMAFHIL ALGLLEEKQQ LQAPPEEV- 937
 Consensus YI..TI...A V.....WE .MLQ...H... ..L.EEKQ. L..A.EE.V. 950

6 mouse_E3 α II TFTFTQKISK PGDAPHNSPS I LAMLETLQN APSLEAHKDM I RWLLKMFNA 998
 4 human_E3 α II TFTFTQKISK PGEAPKNSPS I LAMLETLQN APYLEVHKDM I RWLLKTFNA 998
 15 mouse_E3 α I AFDFYHKASR LGSSANNAQN I QMLLERLKG I PLEGOKDM ITW LQMFDT 987
 2 human_E3 α I TFDFYHKASR LGSSAMNI QML--LEKLKG I PLEGOKDM ITW LQMFDT 984
 Consensus TF.F..K.S. .G....N... I...LE.L.. .P.LE..KDM I.WL.MF.. 1000

6 mouse_E3 α II IKKIRE--CS SSSPVAEAEG TI MEESSRDK DKAERKRKAE I ARLRREKIM 1046
 4 human_E3 α I VKKMR--SS PTSPAETEG TI MEESSRDK DKAERKRKAE I ARLRREKIM 1046
 15 mouse_E3 α I VKRLREKSCLVVATTSGLEC IKSEETHDK EKAERKRKAE AARLHRQKIM 1037
 2 human_E3 α I VKRLREKSCLVVATTSGES IKNDETHDK EKAERKRKAE AARLHRQKIM 1034
 Consensus VK..RE..C.E. ...EE...DK .KAERKRKAE .ARL.R.KIM 1050

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Figure 1H

6	mouse_E3 α II	AQMSQMRRHF	I	DENKELFQQ	TLELDTSASA	TL--DSSPPV	SDAALTALGP	1094		
4	human_E3 α II	AQMSQMRRHF	I	DENKELFQQ	TLELDASTA	VL--DHSPPV	SDMTLTALGP	1094		
15	mouse_E3 α I	AQMSALQKNF	I	ETHKLMYDN	TSEVTGKEDS	I	NEESTSAV	SEASRIALGP	1087	
2	human_E3 α I	AQMSALQKNF	I	ETHKLMYDN	TSEMPGKEDS	I	NEESTPAV	SDYSRIALGP	1084	
	Consensus	AQMS..Q..F	I...	K.....	T.E.....	S.P.V	SD....	ALGP	1100
6	mouse_E3 α II	AQTQVPEPRQ	F	VTCILCOEE	QEVTVGSRAM	VLAAFVQRST	VLSKDRITKI	1144		
4	human_E3 α II	TQTQVPEQRQ	F	VTCILCOEE	QEVKVESRAM	VLAAFVQRST	VLSKNRSKFI	1144		
15	mouse_E3 α I	KRGPAVTEKE	V	LTCILCOEE	QEVKLENNAM	VLSACVQKST	ALTQHRGKPV	1137		
2	human_E3 α	KRGPSVTEKE	V	LTCILCOEE	QEVKIENNAM	VLSACVQKST	ALTQHRGKPI	1134		
	Consensus	TCILCOEE	QEVK.E..AM	VL.A.VQ.ST	.L...R.K.I	1150		
6	mouse_E3 α II	AD-PEKYDPL	F	MHPDLSGCT	HTGSCGHVMH	AHCWQRYFDS	VQAKEQRRQQ	1193		
4	human_E3 α II	QD-PEKYDPL	F	MHPDLSGCT	HTSSCGHIMH	AHCWQRYFDS	VQAKEQRRQQ	1193		
15	mouse_E3 α I	DHLGETLDPL	F	MDPDLAHGT	YTGSCGHVMH	AVCWQKYFEA	VQ---LSSQQ	1184		
2	human_E3 α I	ELSGEALDPL	F	MDPDLAYGT	YTGSCGHVMH	AVCWQKYFEA	VQ---LSSQQ	1181		
	Consensus	...E..DPL	FM	PDL..GT	.TGS	CGHVMH	A.CWQ.YF..	VQ.....	QQ	1200

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Figure 11

6	mouse_E3 α II	RLRLHTSYDV	ENGEEFLCPLC	ECLSNVTI PL	L-LPPRSI LS	RRLN-FSDQP	1241
4	human_E3 α II	RLRLHTSYDV	ENGEEFLCPLC	ECLSNVTI PL	L-LPPRNI FN	NRLN-FSDQP	1241
15	mouse_E3 α I	RI HVDL-FDL	ESGEYLCPLC	KSLCNTVI PI	I PLQPQKI NS	ENAEAL AQL L	1233
2	human_E3 α I	RI HVDL-FDL	ESGEYLCPLC	KSLCNTVI PI	I PLQPQKI NS	ENADAL AQL L	1230
	Consensus	R.....D.	E.GE.LCPLC	..L.NTVI P.	..L.P..I.S	1250
6	mouse_E3 α II	DLAQWRAVT	QQI KVVQML R	RKHNAA-DTS	SSEDEAMNI	I PI PEGFRPD	1290
4	human_E3 α II	NLTQW RTI S	QQI KALQFL R	KEESTP-NNA	STKNSENVDE	LQL PEGFRPD	1290
15	mouse_E3 α I	TLARW QTVL	ARI SGYNI KH	AKGEAPAVPV	LFNOGMGDS	FEFHSI LSFG	1283
2	human_E3 α I	TLARW QTVL	ARI SGYNI RH	AKGENP-I PI	FFNOGMGDS	LEFHSI LSFG	1279
	Consensus	.LA.W.TV.	..I.....	.K..P-..	1300
6	mouse_E3 α II	FYPRNPYSDS	I KEMLTTFGT	AAYKVGLKVH	PNEGDP RVP I	LCWGTCA YTI	1340
4	human_E3 α II	FRPKI PYSES	I KEMLTTFGT	ATYKVGLKVH	PNEEDP RVP I	MCWGS CAYTI	1340
15	mouse_E3 α I	VQSSVKYSNS	I KEMWLFAT	TI YRI GLKVP	PDELDP RVP M	MTWSTCAFTI	1333
2	human_E3 α I	VESSI KYSNS	I KEMWLFAT	TI YRI GLKVP	PDERDP RVP M	LTWSTCAFTI	1329
	ConsensusYS.S	I KEM..F.T	..Y..GLKV.	P.E.DP RVP.	..W.TCA.TI	1350

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SEQ ID NO:									
6 mouse_E3αII	QSIERILSDE	EKPVFGPLPC	RLDDCLRSLT	RFAAAHWTVA	LLPVVQGHC	1390			
4 human_E3αII	QSIERILSDE	DKPLFGPLPC	RLDDCLRSLT	RFAAAHWTVA	SVSVVQGHFC	1390			
15 mouse_E3αI	QAIENTLLGDE	GKPLFGALQN	RQHSLKALM	QFAVAQRATC	PQVLIHKHLA	1383			
2 human_E3αI	QAIENTLLGDE	GKPLFGALQN	RQHNGLKALM	QFAVAQRITC	PQVLIQKHVL	1379			
Consensus	Q . IE . . L . DE	. KPLFG . L . .	R L . . L .	. FA . A Q . H . .	1400			
6 mouse_E3αII	KLFASLVPD	SYEDLPCILD	IDMFHLLVGL	VLAFPALQCQ	D---FSGSSL	1437			
4 human_E3αII	KLFASLVPND	SHEELPCILD	IDMFHLLVGL	VLAFPALQCQ	D---FSGISL	1437			
15 mouse_E3αI	RLLSVILPNL	QSENTPGLLS	VDLFHVLVGA	VLAFPSLYWD	DTVDLQPSPL	1433			
2 human_E3αI	RLLSVLPNI	KSEDTPCLLS	IDLFHVLVGA	VLAFPSLYWD	DPVDLQPSSV	1429			
Consensus	. L PN .	. . E . . PC . L .	ID . FH . LVG .	VLAFP . L . . .	D SSL	1450			
6 mouse_E3αII	ATG--DLHIF	HLVTMAHIVQ	ILLTSCTEEN	---GMDQENP	TGEELAILS	1482			
4 human_E3αII	GTG--DLHIF	HLVTMAHIHQ	ILLTSCTEEN	---GMDQENP	PCEESAVALA	1482			
15 mouse_E3αI	SSSYNHLYLF	HLITMAHMLQ	ILLTTDTDLS	PGPPLAECEE	DSEEARCASA	1483			
2 human_E3αI	SSSYNHLYLF	HLITMAHMLQ	ILLTVDTGL-	---PLAQVQE	DSEEAHSAASS	1475			
Consensus L . . F	HL . TMAH . . Q	ILLT . . T . .	--- Q EE	1500			

SEQ ID NO:

6 mouse_E3αII

4 human_E3αII

15 mouse E3αI

2 human E3 α I

Consensus

6 mouse_E3αII

4 human_E3αII

15 mouse_E3αI

2 human_E3αI

Consensus

6 mouse_E3αII

4 human_E3αII

15 mouse_E3αI

2 human_E3αI

Consensus

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Figure 1K

6	mouse_E3 α I	LHKT	LHQYT	G	SALKEA	PSGW	HLWRSV	RAAI	MPFLKCS	AL	FHYL	NGVP	PAP	1532
4	human_E3 α I	LYKT	LHQYT	G	SALKEI	PSGW	HLWRSV	RAGI	MPFLKCS	ALF	FHYL	NGVP	PSP	1532
15	mouse_E3 α I	FFVEV	SQHTD		GLTGCG	APGW	YLWLSL	RNGI	TPYLRC	AALL	FHYL	LGVA	P	1533
2	human_E3 α I	FFAEI	SQYTS		GSIGCD	IPGW	YLWVSL	KNGI	TPYLRC	AAALF	FHYL	LGVT	PP	1525
	Consensus	QYT.		GW	.LW.S.R.	GI	.P.L.C.	ALF	FHYL.	GV..	P	1550
6	mouse_E3 α II	PDLQV	-SGTS		HFEHLC	NYLS	LPTNLI	HLFQ	ENSDIM	NSLI	ESWC	QNSE	VK	1581
4	human_E3 α II	PDIQV	-PGTS		HFEHLC	SYLS	LPNNLI	CLFQ	ENSEIM	NSLI	ESWC	RNSE	VK	1581
15	mouse_E3 α I	EELFAN	SAEG		EFSALC	SYLS	LPTNLF	LLFQ	EYWDTI	RPLL	QRWC	GDP	PALL	1583
2	human_E3 α I	EELHTN	SAEG		EYSALC	SYLS	LPTNLF	LLFQ	EYWDTV	RPLL	QRWC	ADP	PALL	1575
	Consensus	..L....	S....		.F..	LCSYLS	LPTNL..	LFQ	E...DL.	..WC		1600
6	mouse_E3 α II	RYLNGE	RGA	I	SYPRGA	NKLI	DLPE	DYSSLI	NQASNF	FSCPK	SGGD	KSR	APT	1631
4	human_E3 α II	RYLEGE	RDA	I	RYPRES	NKLI	NLPED	DYSSLI	NQASNF	FSCPK	SGGD	KSR	APT	1631
15	mouse_E3 α I	KSLKQK	SAV	V	RYPRKR	NSLI	ELPE	DYSCLL	NQASHF	RCP	SADDER	KHPV		1633
2	human_E3 α I	NCLKQK	NTV	V	RYPRKR	NSLI	ELPD	DYSCLL	NQASHF	RCP	SADDER	KHPV		1625
	Consensus	..L.....			RYPR..	N.LI	.LPEDYS	.L.	NQAS.F	.CP.	S..D	P.	1650

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Figure 1L

6	mouse_E3 α II	LCLVCGSLLC	SQSYCCQAEI	EGEDVGACTA	HTYSCGSGAG	I FLRVRECQV	1681
4	human_E3 α II	LCLVCGSLLC	SQSYCCQTEL	EGEDVGACTA	HTYSCGSGVG	I FLRVRECQV	1681
15	mouse_E3 α I	LCLFCGAILC	SQNI CCQEIV	NGEEVGACVF	HALHCGAGVC	I FLKI RECRV	1683
2	human_E3 α I	LCLFCGAILC	SQNI CCQEIV	NGEEVGACIF	HALHCGAGVC	I FLKI RECRV	1675
	Consensus	LCL.CG..LC	SQ..CCQ...	.GE.VGAC..	H...CG.GV.	I FL...REC.V	1700
6	mouse_E3 α II	LFLAGKTKGC	FYSPPYLDDY	GETDQGLRRG	NPLHLCQERF	RKI QKLWQQH	1731
4	human_E3 α II	LFLAGKTKGC	FYSPPYLDDY	GETDQGLRRG	NPLHLCCKERF	KKI QKLWHQH	1731
15	mouse_E3 α I	VLVEGKARGC	AYPAPYLDEY	GETDPGLKRG	NPLHLSRERY	RKLHLVWQQH	1733
2	human_E3 α I	VLVEGKARGC	AYPAPYLDEY	GETDPGLKRG	NPLHLSRERY	RKLHLVWQQH	1725
	Consensus	...GK...GC	.Y..PYLD.Y	GETD.GL.RG	NPLHL...ER.	RK...WQQH	1750
6	mouse_E3 α II	SITEEI GHAQ	EANQTLVGID	WQHL			1755
4	human_E3 α II	SVTEEI GHAQ	EANQTLVGID	WQHL			1755
15	mouse_E3 α I	CIIEEI ARSQ	ETNQMLFGFN	WQLL			1757
2	human_E3 α I	CIIEEI ARSQ	ETNQMLFGFN	WQLL			1749
	Consensus	.I.EEI...Q	E.NQ.L.G..	WQ.L			1774

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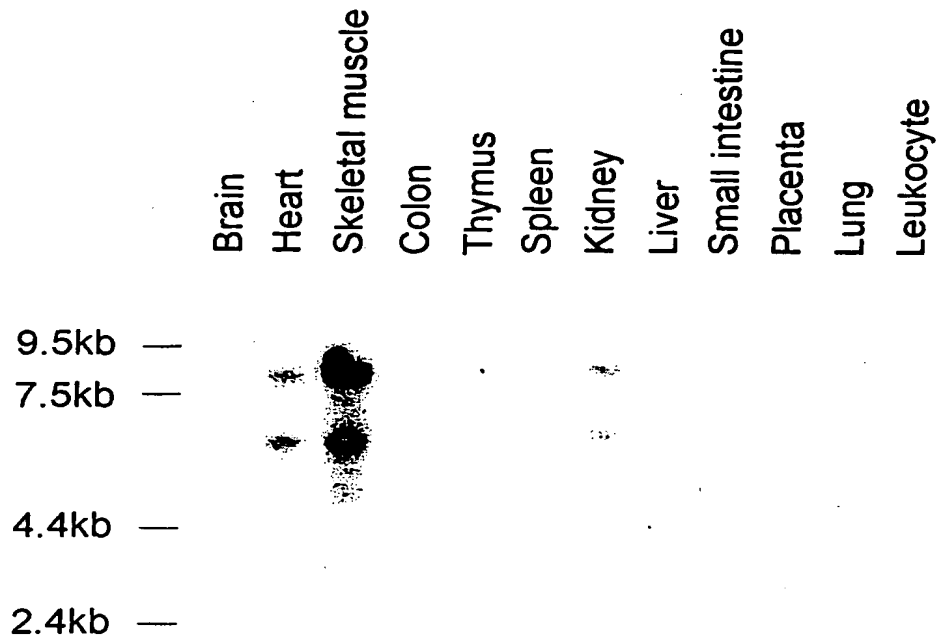
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FIG. 2

**Tth Expression Profile of huE3 α -II
in Human Tissues**



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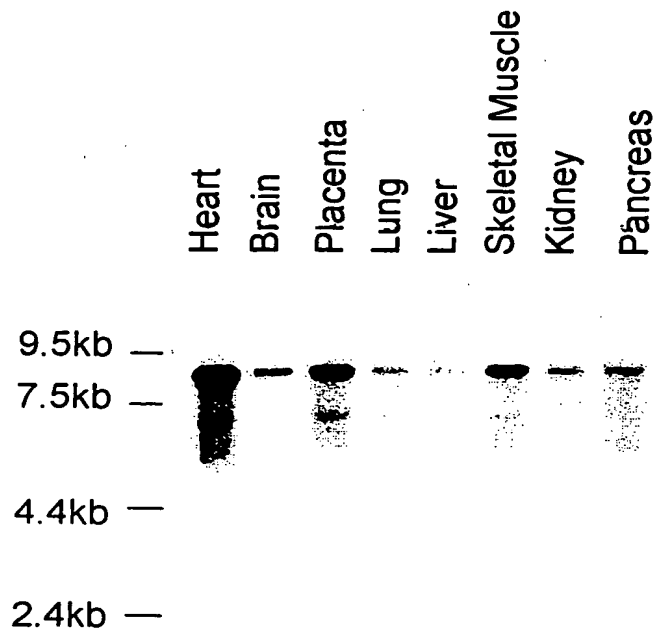
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FIG. 3

**Tth Expression Profile of huE3 α -I
in Human Tissues**



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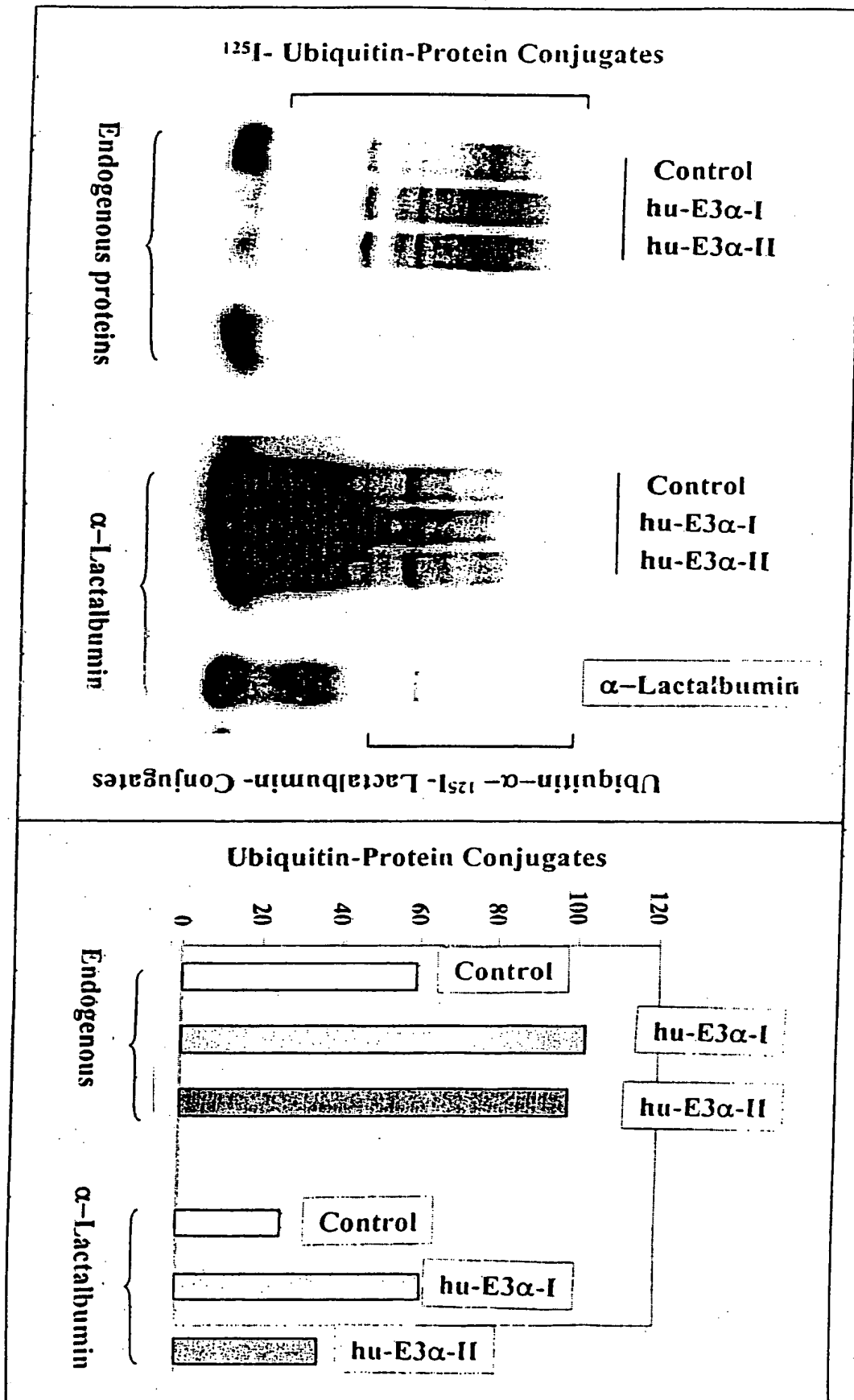
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Ubiquitination of Endogenous Proteins

Figure 4

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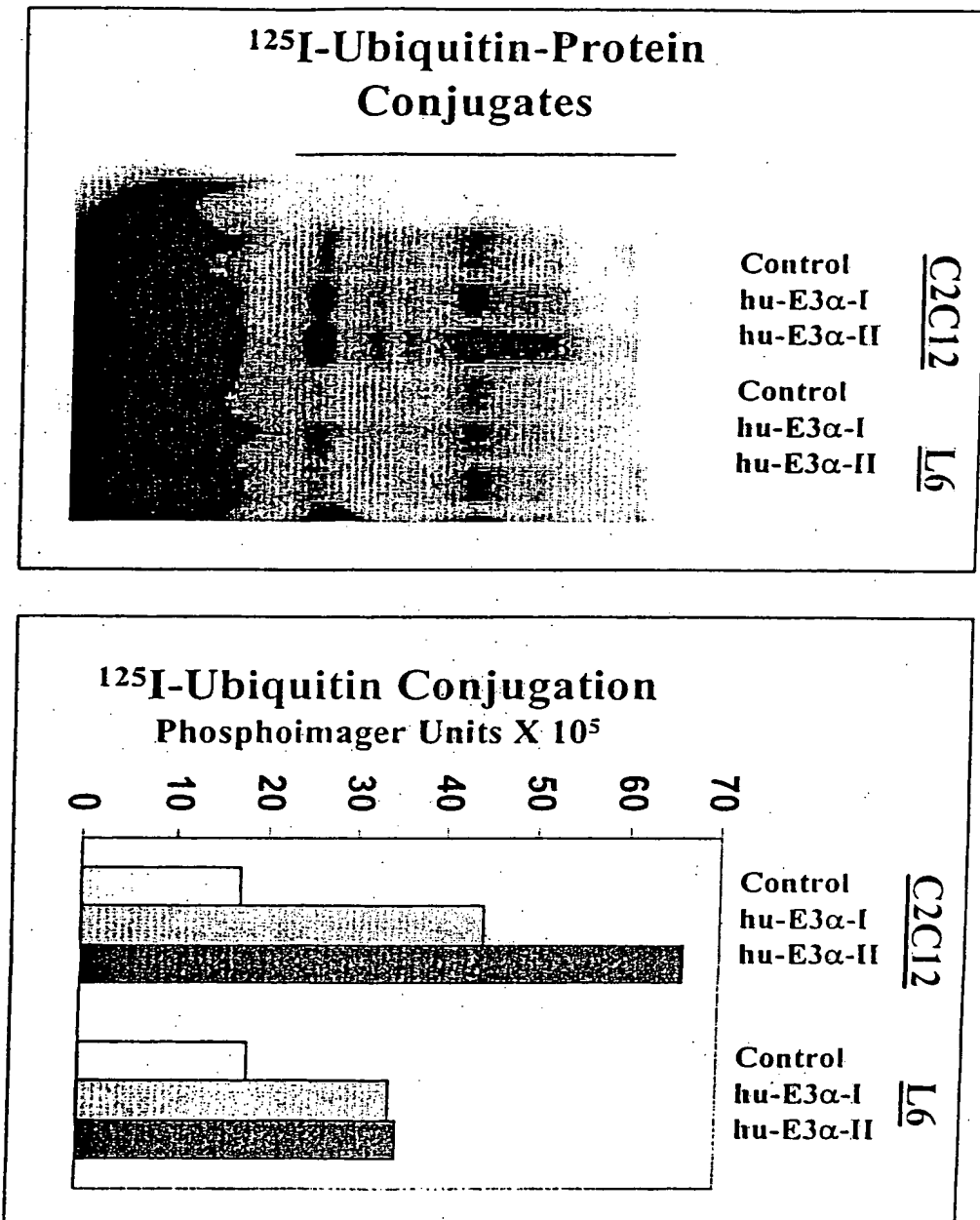
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Figure 5

Transfection of Human E3 α -I or E3 α -II cDNA Stimulates Ubiquitin Conjugation in Cultured Muscle Cell Lines



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Figure 6

¹²⁵I-Ubiquitin Conjugation to Muscle Proteins and Its Sensitivity to E3 α Inhibitor
in Skeletal Muscle Extracts

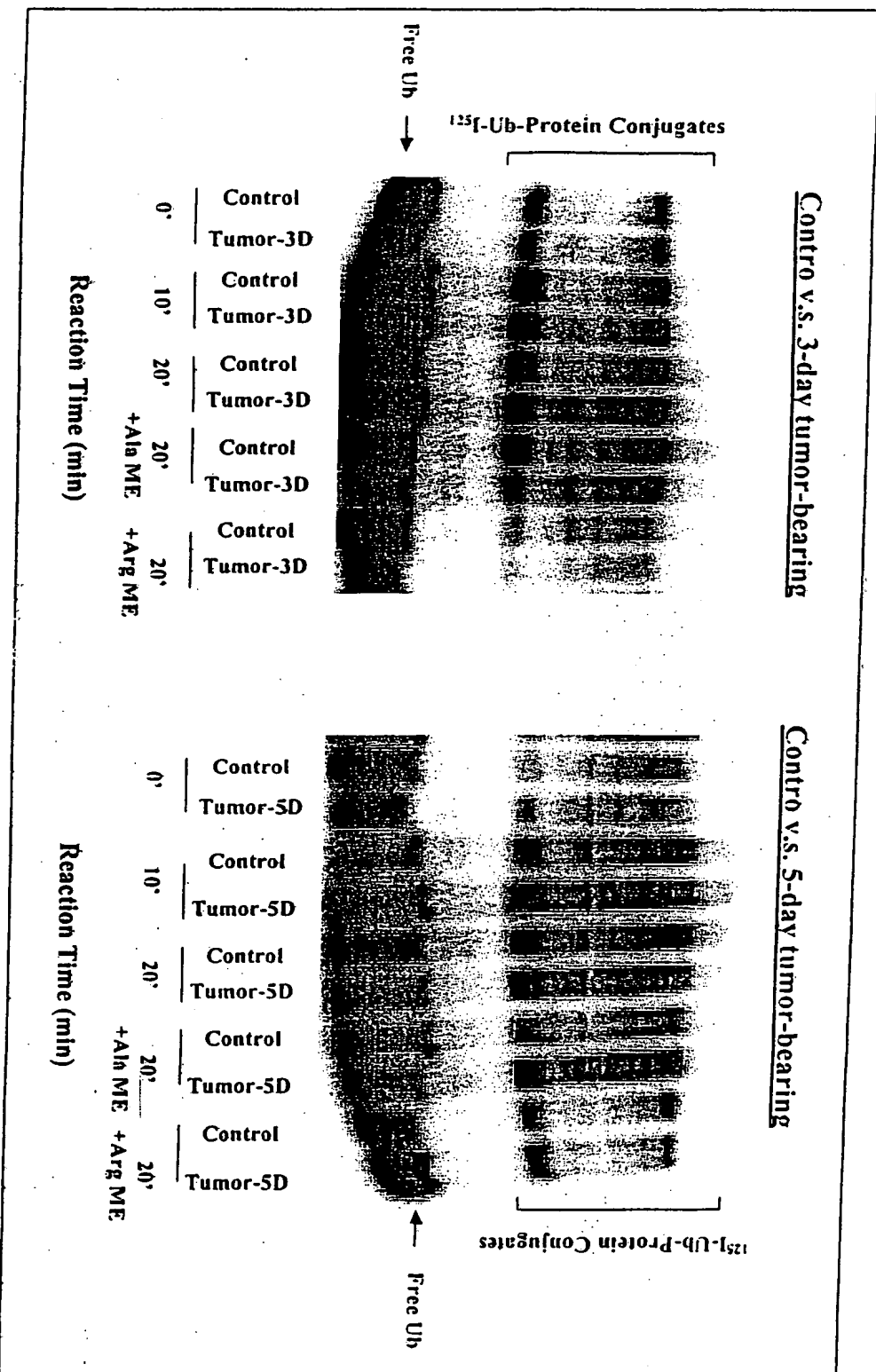
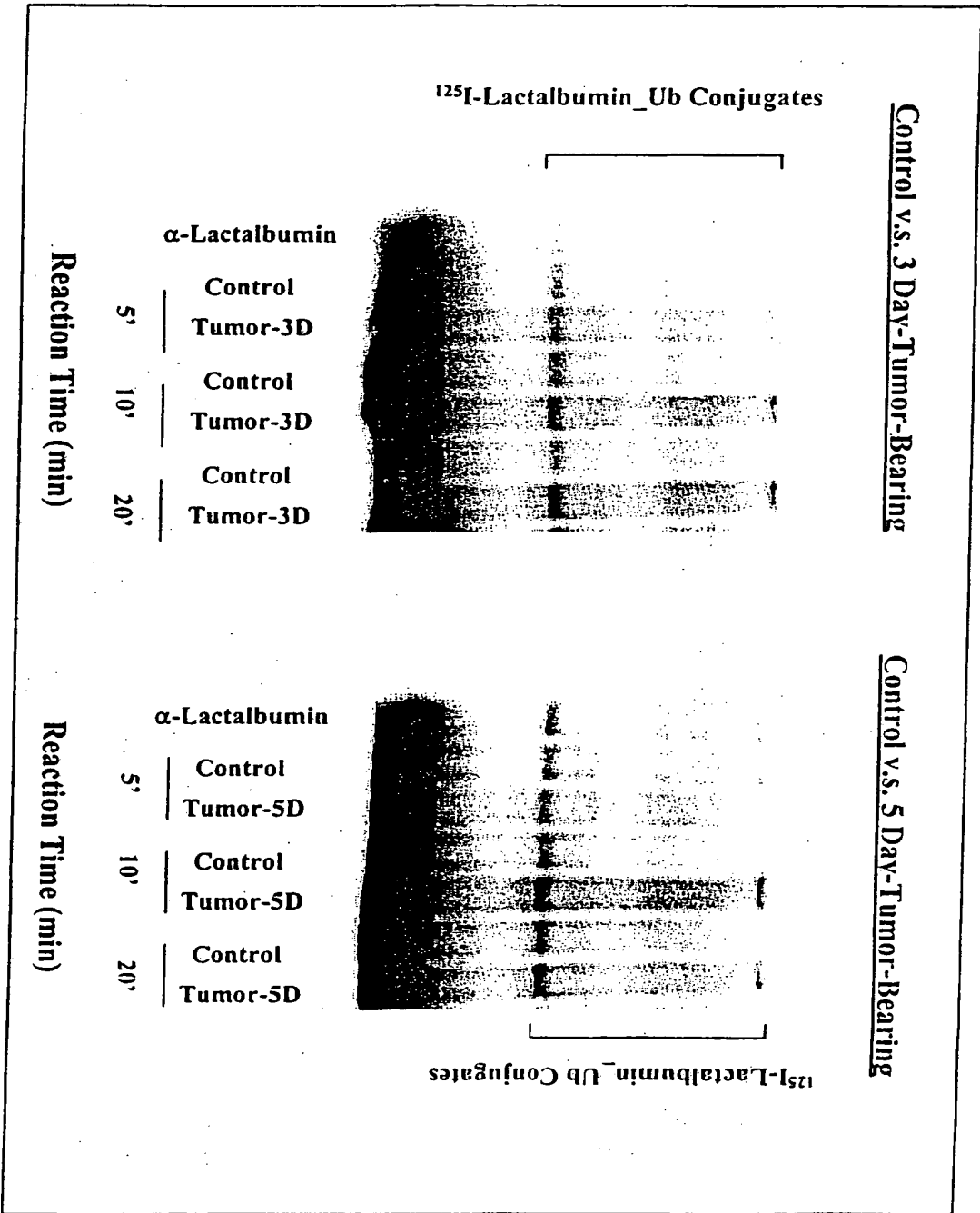


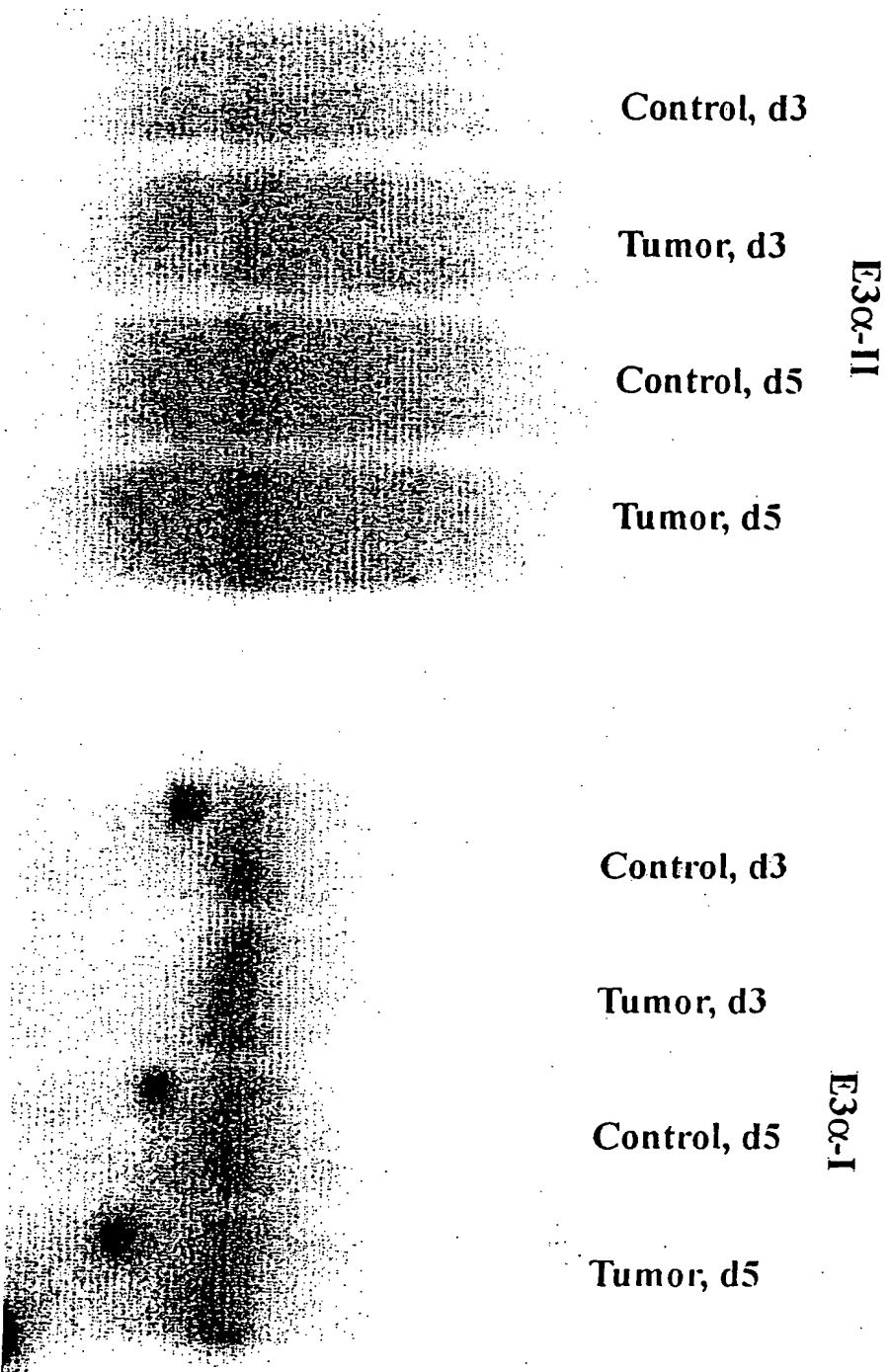
Figure 7
 Rates of Ubiquitination of N-end Rule Substrate
 α -Lactalbumin in Skeletal Muscle Extracts
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Figure 8

**Northern blot analysis of E3 α -I & E3 α -II expression
in gastrocnemius muscles in YAH-130 experimental cachexia model**



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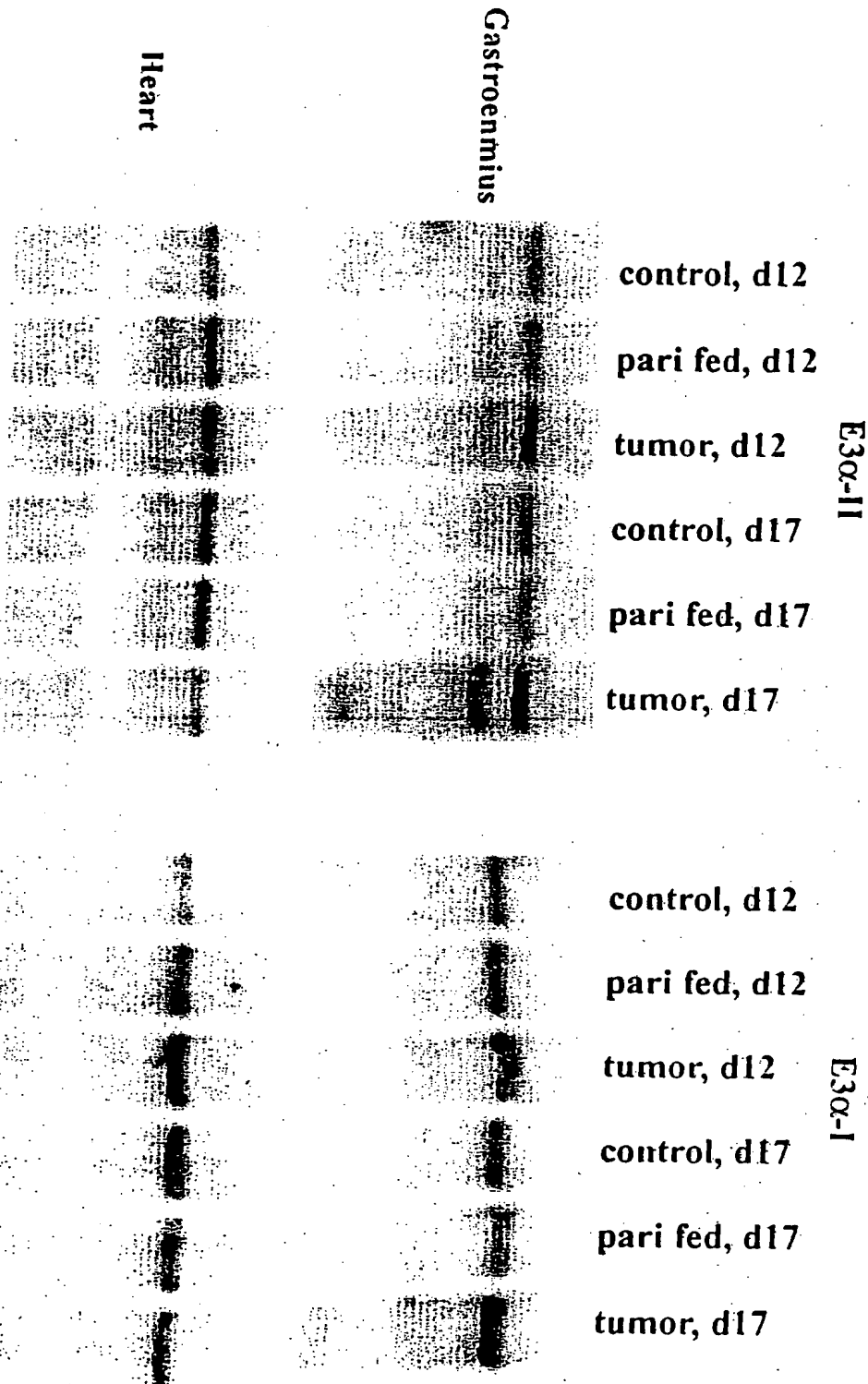
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Figure 9

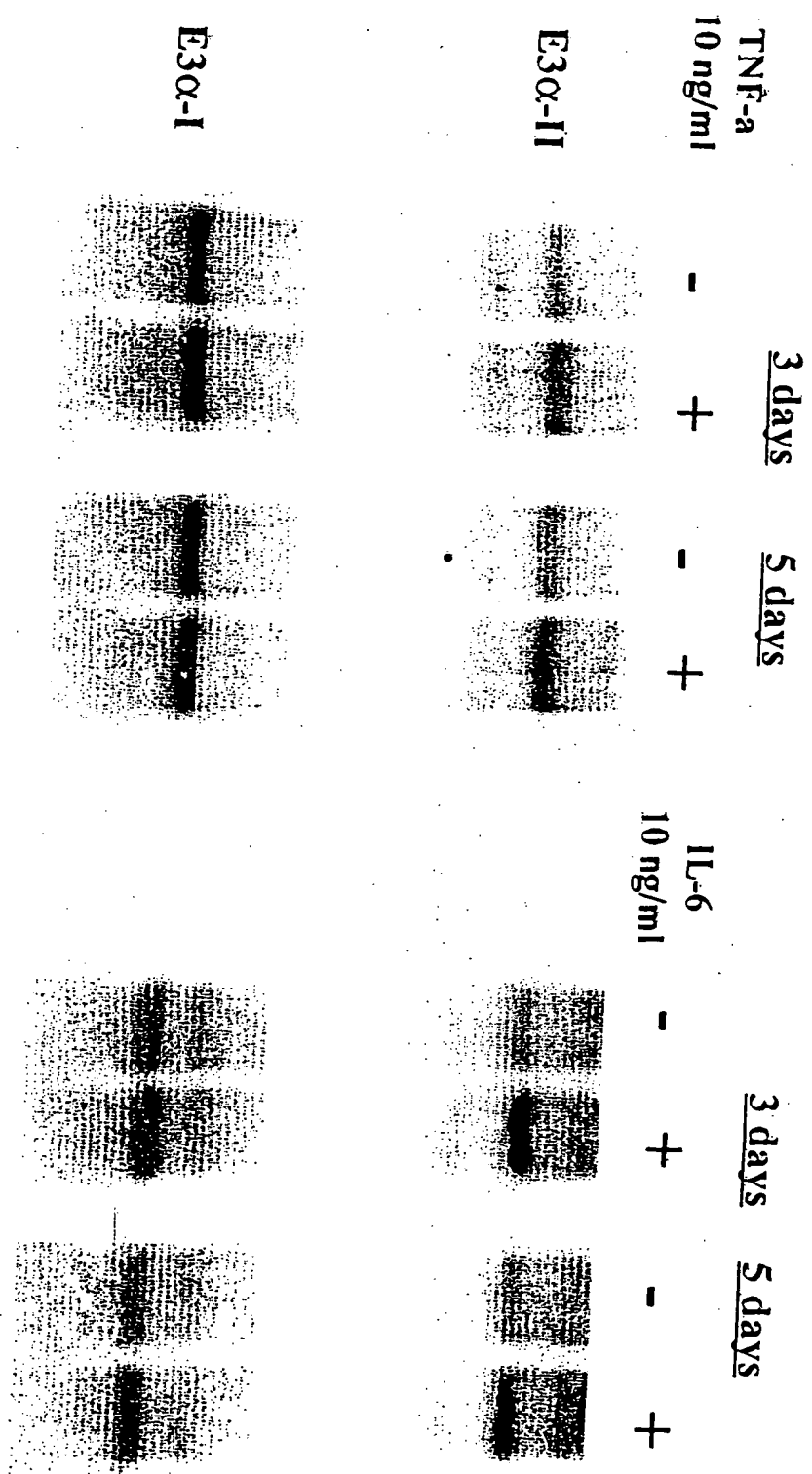
**Northern blot analysis of E3 α -I and E3 α -II expression in
gastrocnemius muscle and cardiac muscle
in C26 experimental cachexia model**



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Figure 10

Proinflammatory cytokines TNF- α and IL-6
 induce E3 α -II Expression in C2C12 myotube culture



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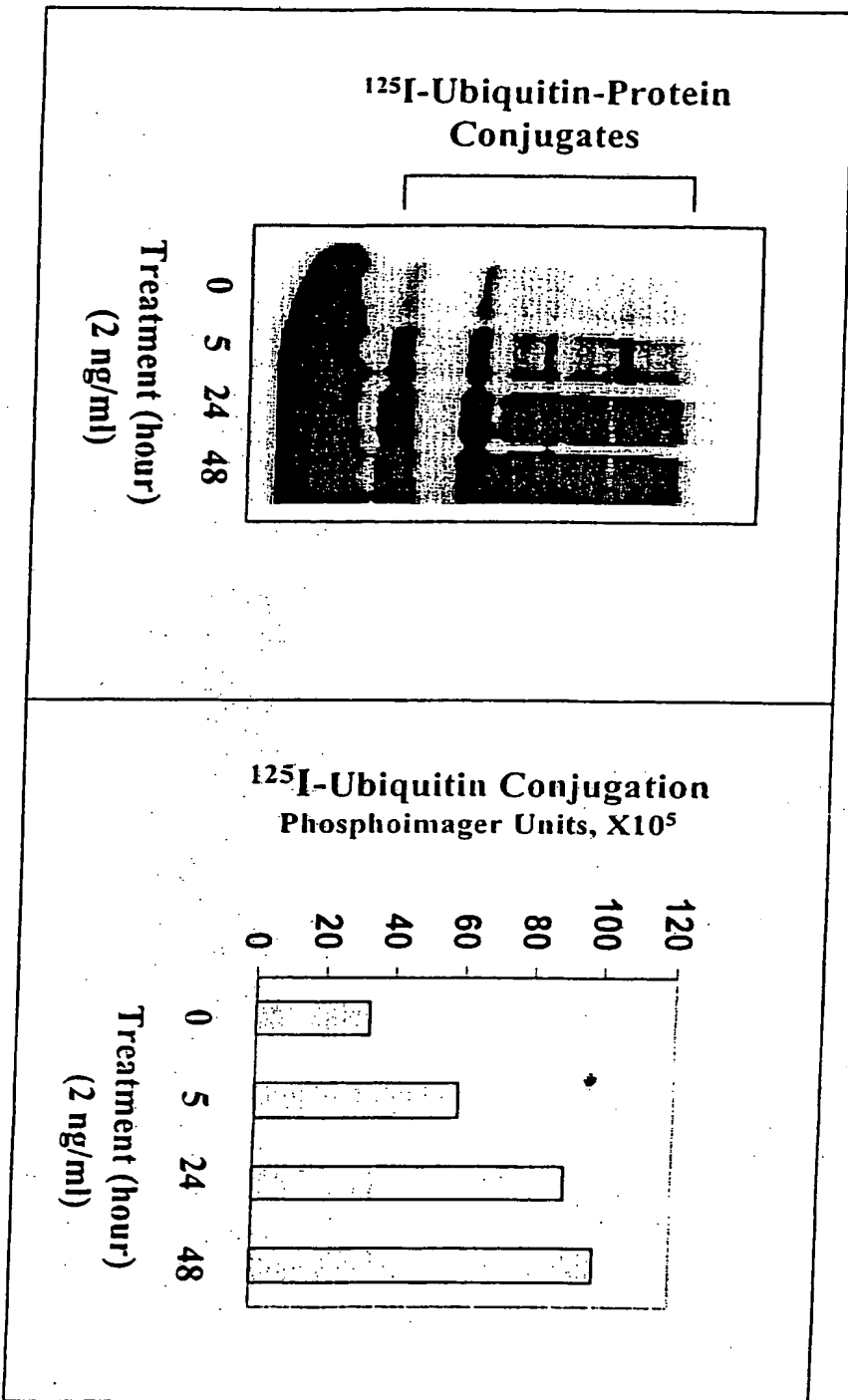
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Fig. 11 (Page 22 of 23)

Figure 11

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IL-6 Elicits Accelerated Ubiquitination in C2C12 Myotube Cultures



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Figure 12

TNF α Elicits Accelerated Ubiquitination in C2C12 Myotube Cultures

